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Determinants of the Need for Early Acute Intervention in Patients Treated Conservatively After Thrombolytic Therapy for Acute Myocardial Infarction

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This study sought to determine whether clinical variables can be used to identify patients at high risk of recurrent spontaneous myocardial ischemia or hemodynamic compromise during the 1st 4 days after intravenous thrombolysis for acute myocardial infarction. Of 288 patients randomly assigned to a conservative postthrombolysis strategy, 54 (19%) required urgent cardiac catheterization within 24 h; 75 (26%) underwent urgent cardiac catheterization within 4 days of admission. Of the clinical variables examined by multiple logistic regression analysis, only patient age and anterior wall myocardial infarction correlated with the need for urgent cardiac catheterization ($p = 0.0016$ and $p = 0.017$, respectively). Compared with recombinant tissue-type plasminogen activator or urokinase monotherapy, combination therapy with these agents was associated with a lower need for acute intervention during the 1st 24 h after admission, but the difference did not reach statistical significance (14% for combination therapy vs. 21% for each agent alone, $p = 0.30$).

Of the 75 patients undergoing urgent coronary angiography, only 39% had an occluded infarct-related artery. Emergency coronary angioplasty was performed in 49% of the patients and coronary artery bypass graft surgery was performed urgently in 3%. Despite these interventions, the need for urgent cardiac catheterization was associated with an in-hospital mortality rate of 7% (vs. 3% in the group not requiring urgent angiography, $p = 0.36$); mean left ventricular ejection fraction was 50.5 ± 11% (vs. 54.3 ± 10.8%, $p = 0.12$) and regional infarct zone wall motion was −2.68 ± 1.07 SD/chord (vs. −2.46 ± 1.19 SD/chord; $p = 0.44$).

These data suggest that a relatively large proportion of patients treated conservatively after thrombolytic therapy require early triage to urgent coronary angiography; 2) baseline clinical characteristics are poorly predictive of the need for urgent intervention; and 3) despite ready access to facilities for aggressive intervention, the in-hospital clinical outcome of this group of patients appears to be poorer than that of patients without recurrent ischemia or hemodynamic instability.

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Optimal management of acute myocardial infarction after the early administration of fibrinolytic therapy remains controversial. The value of immediate coronary angioplasty of residual infarct-related vessel stenosis was investigated in three randomized controlled clinical trials (2–4). In contrast to earlier nonrandomized studies, which suggested that this strategy reduced the risk of reocclusion and reinfarction (5) and improved the rate and extent of left ventricular functional recovery (6), each of these three trials concluded that immediate coronary angioplasty after successful recombinant tissue-type plasminogen activator (rt-PA) therapy was associated with a higher incidence of procedural complications and a higher requirement for blood transfusion than those associated with a deferred angioplasty strategy. The more aggressive strategy also failed to reduce in-hospital morbidity and mortality and was associated with no increase in left ventricular functional recovery.

More recently, the need for any postthrombolytic intervention, including coronary angiography, has been questioned (7,8). This issue was specifically addressed in the Fifth Thrombolysis and Angioplasty in Myocardial Infarc-

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tion trial (TAMI-5) (1). In this randomized controlled study, three intravenous thrombolytic regimens (rt-PA alone, urokinase alone and combined urokinase and rt-PA) were compared. In addition, patients enrolled in the study were randomly allocated to either immediate or delayed predischarge coronary angiography. The overall findings of the trial have been previously published (1). The principal aim of the present analysis was to determine whether clinical variables available at the time of admission can be used to identify the subgroup of patients allocated to a strategy of deferred angiography who are likely to subsequently require urgent cardiac catheterization for recurrent myocardial ischemia or hemodynamic compromise. The ability to predict this need would have important implications for patient management, particularly for the triage of patients presenting to community hospitals. The secondary aim of the study was to compare the clinical outcome of this group of patients with that of patients who remained in stable condition throughout the hospital course.

Methods

Patient selection. Between April 1988 and May 1989, 575 patients were enrolled in the TAMI-5 study. Patients were eligible for recruitment if they presented to one of the participating institutions (7 main centers and 20 community hospitals) within 6 h of symptom onset and had associated unequivocal electrocardiographic (ECG) changes of acute myocardial infarction. These changes included ≥0.1-mV ST segment elevation in two or more contiguous leads or ST segment depression in leads V_1 to V_4 consistent with posterior wall infarction. Patients were ineligible for enrollment if they were >75 years of age and had a history of previous coronary artery bypass graft surgery or prior Q wave myocardial infarction in the same myocardial distribution. They were also excluded if they had contraindications to thrombolysis, including recent active genitourinary or gastrointestinal bleeding, recent major surgery or organ biopsy, previous stroke or transient ischemic episode, uncontrolled hypertension or prolonged cardiopulmonary resuscitation. In addition, patients were excluded if, on admission, they were in: cardiogenic shock, defined as a systolic blood pressure <80 mm Hg in the presence of an adequate left ventricular filling pressure.

Treatment regimen. Using a 3 × 2 factorial design, each patient enrolled in the study was randomly assigned to one of three thrombolytic regimens and to one of two interventional strategies. The thrombolytic agents employed were rt-PA and urokinase, given alone or in combination. When given alone, rt-PA was administered intravenously as a bolus dose of 10 mg followed by 50 mg over the next 1 h and an additional 20 mg during each of the next 2 h for a total dose of 100 mg. Urokinase, when given alone, was infused at a rate of 1.5 million U over 2 min, followed by an additional 1.5 million U over the next 1 h. When given in combination, rt-PA, 1 mg/kg, was given over 1 h (10% as an initial bolus dose, with a maximal total dose of 90 mg) with urokinase, 1.5 million U, over 1 h through a separate intravenous infusion line.

After allocation to a thrombolytic regimen, each patient was randomly assigned to either immediate cardiac catheterization and mechanical reperfusion therapy (coronary angioplasty or coronary artery bypass graft surgery) as considered necessary (n = 287), or to deferred predischarge cardiac catheterization (n = 288). Those patients allocated to the immediate cardiac catheterization strategy were transferred to the catheterization laboratory as soon as possible after enrollment. Coronary patency was determined 90 min after the initiation of the thrombolytic infusion. Patients with a persistently occluded infarct-related artery (Thrombolysis in Myocardial Infarction trial [TIMI] flow grade 0 or 1) 90 min after the initiation of fibrinolytic therapy were considered for rescue coronary angioplasty if they had suitable coronary anatomy. Patients with ongoing myocardial ischemia and anatomy deemed unsuitable for coronary angioplasty were referred for urgent coronary artery bypass graft surgery. Repeat cardiac catheterization was performed before hospital discharge to evaluate changes in global and regional left ventricular function and to document infarct-related vessel patency.

The 288 patients allocated to the alternative, more conservative strategy of delayed catheterization were admitted to the coronary care unit and treated with a prespecified medical regimen that included intravenous lidocaine, intravenous heparin, an oral calcium channel antagonist and aspirin. A beta-adrenergic blocking agent was not given routinely but was prescribed as indicated for systemic hypertension, recurrent ischemia or supraventricular tachycardia. Patients in this group did not undergo cardiac catheterization until 5 to 10 days after admission unless they developed one or more of the following: 1) recurrent myocardial ischemia, defined as recurrent ischemic chest pain lasting >20 min; 2) new ST-T wave changes; 3) new mitral regurgitation or clinical evidence of moderate or severe acute pulmonary edema; and 4) persisting hypotension, defined as a systolic blood pressure <90 mm Hg (or the need for inotropic support) for >1 h. To facilitate the identification of factors that may predict the need for urgent cardiac catheterization, the clinical characteristics of the patients who remained in stable condition throughout their hospital course were compared with the characteristics of the group requiring urgent cardiac catheterization within 24 h and with the total group requiring intervention during the 1st 4 days after admission. For the sake of simplicity, these latter groups are referred to as having "crossed over" to emergency cardiac catheterization from the intended conservative management plan.

Cardiac catheterization. In all patients, contrast left ventriculography was performed in the 30° right anterior oblique projection. Global left ventricular ejection fraction and regional wall motion analyses were performed with use of the area-length (9) and centerline chord (10) methods, respec-

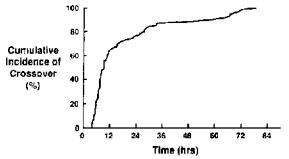


Figure 1. Cumulative incidence of crossover to acute intervention during the 1st 4 days after hospital admission in 75 patients.

tively. End-diastolic and end-systolic frames were selected for analysis by an experienced observer unaware of the patient's assigned thrombolytic regimen or intervention strategy. Selective coronary angiography was performed in multiple left and right anterior oblique projections and the severity of coronary artery stenosis was quantitatively determined using a validated computer-automated system (11).

Statistics. All values are expressed as mean values ± 1 SD or median (25th and 75th percentiles) unless otherwise stated. Global left ventricular function and regional wall motion were compared between the groups with the Wilcoxon rank-sum test; chi-square analysis was used to compare mortality rates. Sixteen clinically derived variables were selected for univariable logistic regression analysis to identify factors associated with the need for urgent invasive evaluation and coronary intervention; five variables that appeared to be associated with the need for crossover were then selected for inclusion in a multivariable logistic regression analysis. A two-tailed probability (p) value <0.05 was considered to be statistically significant.

Results

Baseline demographics and treatment regimen. Of the 288 patients randomly assigned to the relatively conservative delayed cardiac catheterization strategy, 75 (26%) underwent urgent cardiac catheterization for recurrent myocardial ischemia or hemodynamic instability during the 1st 4 days after admission, with a median time to crossover of 9 h (25th and 75th percentiles = 7 and 23 h, respectively) (Fig. 1); in the majority of these patients (72%), cardiac catheterization was performed within 24 h of admission. Baseline demographic variables and admission hemodynamics for the patients not requiring urgent cardiac catheterization, those requiring angiographic evaluation within 24 h and those crossing over to urgent angiography during the 1st 4 days after admission are compared in Table 1. No differences are apparent among the groups in gender distribution or presence of certain risk factors for coronary artery disease, including cigarette smoking, hyperlipidemia and systemic hypertension. Urgent cardiac catheterization was performed slightly more frequently in patients with diabetes mellitus (28% vs. 17%). There were no differences in admission heart rate or systemic blood pressure among the three groups (Table 1). Similarly, there was no difference in the likelihood of crossover according to the site of recruitment (Fig. 2). Those patients who initially presented to a community hospital were referred for urgent cardiac catheterization equally as often as patients presenting to one of the larger referral centers (25% vs. 28%). Urgent angiography was performed more frequently, however, after acute anterior than after acute inferior wall infarction (32% vs. 22%, $p = 0.04$).

Influence of treatment and clinical variables (Table 2). No group differences were apparent in the time from the onset of

Table 1. Baseline Demographic Characteristics and Admission Hemodynamics of 288 Patients

	Crossover <1 Day (n = 54)	Crossover ≤4 Days (n = 75)	No Crossover (n = 213)
Age (mean ± SD) (yr)	57.4 ± 8	58.5 ± 8	58.1 ± 10.4
% Men	74	71	75
Coronary risk factors (%)			
Diabetes mellitus	28	28	17
Systemic hypertension	30	35	44
Hyperlipidemia	25	26	31
Cigarette smoking	63	55	62
Prior myocardial infarction (%)	9	9	12
Rest angina (%)	28	25	22
ECG infarct location (%)			
Anterior	56	52	39
Inferior	44	48	61
Admission hemodynamic values (mean ± SD)			
Pulse rate (beats/min)	75 ± 17	77 ± 18	76 ± 17
Systolic pressure (mm Hg)	127 ± 22	132 ± 25	131 ± 24
Diastolic pressure (mm Hg)	78 ± 16	81 ± 17	81 ± 16

ECG = electrocardiographic.

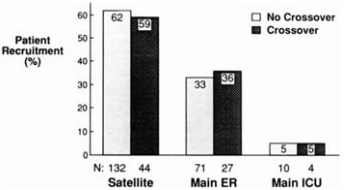


Figure 2. Relation between site of patient recruitment and referral for urgent cardiac catheterization. The likelihood of crossover was the same at peripheral sites as at the main centers. ER = emergency room; ICU = intensive care unit.

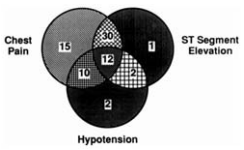


Figure 3. Indications for urgent cardiac catheterization in 72 patients.

symptoms to initiation of thrombolytic therapy. Although the difference was not statistically significant ($p = 0.30$), the need for crossover during the 1st 24 h after admission was less frequent after combined urokinase and rt-PA therapy (14%) than after monotherapy with either agent alone (21%). This difference was less apparent by the 4th hospital day (combined therapy 22% vs. urokinase 26% vs. rt-PA 30%, $p = 0.40$). Identification of the infarct-related artery did not predict the need for urgent cardiac catheterization. Crossover occurred in 31% of patients with an infarct in the territory of the left anterior descending coronary artery, 27% of patients with a right coronary artery-related infarct and 24% of patients with a left circumflex coronary artery-related infarct. Of the 85 patients in whom the left anterior descending artery was the infarct-related artery, 25% crossed over within the 1st 24 h of admission. This compares with 11% of the patients with a circumflex artery-related infarct and 18% of those with an infarct in the territory of the right coronary artery. Similarly, the presence of multivessel coronary artery disease, defined as the presence of ≥70% stenosis of the coronary lumen diameter in two or more of the major epicardial coronary arteries, was not predictive of the need for urgent cardiac catheterization (28% vs. 44% within 4 days of admission).

Indications for emergency cardiac catheterization (Fig. 3). In the majority of patients, the primary indication for emergency cardiac catheterization was recurrent ischemic chest pain. Approximately 60% of the patients had new ECG changes consistent with myocardial ischemia and 80% had either new ECG changes or hemodynamic compromise. Of those crossing over within 24 h of admission, systolic hypotension was documented in 40% and acute pulmonary edema occurred in 25%.

Table 2. Thrombolytic Therapy and Angiographic Findings in 288 Patients

	Crossover <1 Day (n = 54)	Crossover ≤4 Days (n = 75)	No Crossover (n = 213)
Time to therapy (h)	3.1 ± 1.1	3 ± 1.2	3.1 ± 1.2
Treatment group (%)			
Urokinase	21	26	74
rt-PA	21	30	70
rt-PA + urokinase	14	22	78
Time to crossover (h)*	5.7,7.6,10.6	6.5,9.2,23	NA
Infarct-related artery (%)			
Left anterior descending	39	35	29
Right coronary	52	51	56
Left circumflex	8	12	14
Other	2	2	1
Infarct vessel TIMI grade flow (acute cath) (%)			
0	23	29	NA
1	10	10	NA
2	33	29	NA
3	33	32	NA
No. of diseased vessels (%)			
0 to 1	66	72	56
2	23	21	27
3	11	7	17

*25th, 50th or 75th percentile, respectively. Cath = catheterization; NA = not applicable; TIMI = Thrombolysis in Myocardial Infarction trial; rt-PA = recombinant tissue-type plasminogen activator.

Table 3. Clinical Outcome of 288 Patients

Clinical Sequelae	Crossover <1 Day (n = 54)	Crossover ≥4 Days (n = 75)	No Crossover (n = 213)
Pulmonary edema/heart failure (%)	25	24	15
Emergency PTCA (%)*	46	49	NA
Emergency CABG (%)*	0	3	NA
Predischarge CABG (%)	11	15	22
Death (%)	7	7	3

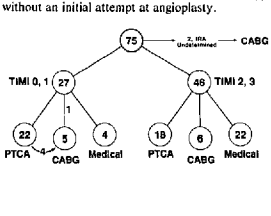
*At the time of crossover angiography. CABG = coronary artery bypass surgery; NA = not applicable; PTCA = percutaneous transluminal coronary angioplasty.

Angiographic findings and clinical outcome (Table 3). Of the 75 patients undergoing emergency coronary angiography, only a minority (39%) had an occluded infarct-related artery (TIMI grade 0 or 1 coronary flow); 32% had TIMI grade 3 coronary flow. The distribution of coronary flow grades was similar in the patients crossing over within 24 h of admission. The patency status of the infarct-related artery was not readily predicted by the nature of the indication for intervention. The infarct-related vessel was patent in 60% of patients with recurrent chest pain, 45% of patients with new ST segment elevation and 23% of patients with systolic hypotension.

Emergency coronary angioplasty was performed at the time of the emergency cardiac catheterization in 37 patients (49%). Of these, one patient died 24 h after the procedure and two required emergency coronary artery bypass graft surgery. An additional 11 patients in the crossover group underwent urgent or elective bypass surgery before hospital discharge (Fig. 4) and 3 patients who were initially treated conservatively at the time of the urgent cardiac catheterization procedure subsequently underwent emergency coronary angioplasty on the next day. Despite the ready availability of these mechanical revascularization procedures, the group requiring urgent intervention appeared to have a poorer clinical outcome than that of the patients who remained free of recurrent myocardial ischemia or hemodynamic compromise. The need for urgent intervention was associated with somewhat poorer predischarge global left ventricular function, particularly in the early crossover group (Fig. 5). The left ventricular ejection fraction in this group was 50.5 ± 11% compared with 54.3 ± 10.8% in the patients who remained in stable condition throughout the hospital course ($p = 0.12$). The severity of regional dysfunction of the infarct zone was marginally greater in the crossover group than in the group without recurrent ischemia or hypotension (−2.68 ± 1.07 vs. −2.46 ± 1.19 SD/chord, $p = 0.44$), but regional function of the noninfarct zone was similar in these two groups (0.35 ± 1.29 vs. 0.24 ± 1.26 SD/chord, $p = 0.55$). The need for urgent cardiac catheterization in the 1st 24 h was associated with an in-hospital mortality rate of 7% compared with 3% in the group remaining stable during this period ($p = 0.32$). Each of the five patients in the crossover group who died had a patent infarct-related artery (TIMI grade 2 or 3 flow) at the time of emergency cardiac catheterization.

Predictive factors (Tables 3 and 5). Sixteen clinical, hemodynamic and treatment variables available to the clinician at the time of admission of the patient to the coronary care unit were used to identify predictors of the need for urgent cardiac catheterization within 4 days after admission to the hospital (Table 4). Of the factors examined, only patient age and anterior infarction were significant variables by multiple logistic regression analysis (Table 5). The association between age and the need for crossover was nonlinear with a progressive increase in frequency with age to a peak incidence in the group of patients aged 60 to 65 years, followed by a decline in frequency in older patients.

Figure 4. Patency status (Thrombolysis in Myocardial Infarction [TIMI] grade flow) of the infarct-related artery (IRA) at urgent cardiac catheterization and subsequent management (emergency and elective treatment) in 75 patients. Percutaneous transluminal coronary angioplasty (PTCA) was attempted but was unsuccessful in four patients who then had elective or emergency coronary artery bypass graft (CABG) surgery. One patient underwent bypass graft surgery without an initial attempt at angioplasty.



Discussion

The principal findings of this study were that 1) urgent cardiac catheterization with or without subsequent mechanical revascularization procedures was performed in a relatively large proportion of patients assigned to a conservative strategy after fibrinolytic therapy, and 2) the need for urgent intervention was poorly predicted by clinically derived variables. Although some investigators (12,13) have objected to the use of the term "crossover" to refer to similar patient subgroups (because the use of emergency cardiac catheterization and mechanical revascularization was an integral component of the prespecified conservative strategy), we

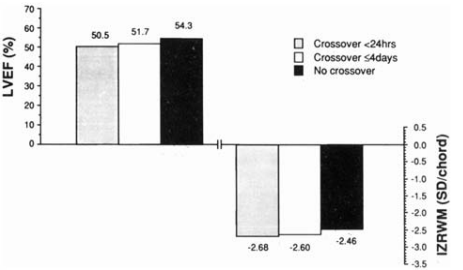


Figure 5. Global and regional left ventricular function at repeat cardiac catheterization 7 days after admission in 288 patients. Although not statistically significant, there was a trend toward better function in the group (n = 213) not requiring urgent cardiac catheterization. IZRWM = infarct zone regional wall motion; LVEF = left ventricular ejection fraction.

have used the term freely for the sake of nomenclatural simplicity.

Frequency of crossover. The frequency of crossover before the 5th hospital day (26%) was somewhat higher in this study than that reported in the Thrombolysis in Myocardial Infarction (TIMI)-2A trial (14) and in the Should We Intervene Following Thrombolysis? (SWIFT) study (8). These randomized studies also evaluated the need for and optimal timing of cardiac catheterization after thrombolytic therapy (rt-PA and anistreplase, respectively). In the TIMI-2A trial (14), 12.2% of 197 patients allocated to a conservative postlytic strategy underwent urgent coronary angiography for recurrent ischemia within 5 days of admission and coronary angioplasty was performed in approximately 50% of these patients. Conversely, in the TIMI-2B trial (6), cardiac catheterization was performed before day 15 in 32.7% of the conservative strategy group (in 25.8% for recurrent myocardial ischemia) and coronary angioplasty and bypass graft surgery were performed in 13.3% and 6.6%, respectively. Thus, the frequency of intervention by day 15 in the latter study was not dissimilar from the crossover rate within 4 days in the current study. In the SWIFT study (8), 13% of the 403 patients assigned to conservative postlytic therapy underwent predischarge coronary angiography and revascularization procedures were performed in only 5%. However, patients enrolled in the SWIFT study were <70 years old and presented within 3 h of their first myocardial infarction and were thus at relatively low risk of early complications. Moreover, randomization to invasive or conservative postlytic therapy was delayed for up to 24 h from the administration of thrombolytic therapy, allowing approximately 8% of eligible patients to be excluded from randomization because of hemodynamic instability. In the current study, urgent cardiac catheterization was performed not only for recurrent myocardial ischemia, but also for clinically significant hemodynamic instability with the expectation that revascularization in the latter group would prevent potentially irreversible myocardial failure. These differences may account for some of the observed differences in frequency of intervention among the studies. It is also likely, however, that because of divergent therapeutic philosophies, the threshold for early acute intervention was lower in the TAMI trial than in the three other studies.

Table 4. Variables Evaluated by Univariable Analysis

Clinical variables
Age
Gender
Diabetes mellitus
Cigarette smoking
Systemic hypertension
Hyperlipidemia
Prior myocardial infarction
Prior angina pectoris
History of rest angina
Prior beta-blocker therapy
Infarct location on electrocardiography
Hemodynamic variables at admission
Pulse rate
Systolic blood pressure
Diastolic blood pressure
Treatment variables
Time to therapy
Thrombolytic agent

Predictive factors. Only 2 of 16 clinically available variables (patient age and anterior wall myocardial infarction) were associated with the need for urgent cardiac catheterization. Each of these is unequivocally associated with an increased morbidity and mortality after acute myocardial

Table 5. Multiple Logistic Regression Analysis: Predictors of the Need for Urgent Cardiac Catheterization Before Day 5 After Hospital Admission

Variable	Univariable Chi-Square	p Value	Multivariable Chi-Square	p Value
Age	9.92	0.019	10.01	0.0016
Anterior myocardial infarction	4.60	0.032	5.66	0.017
Diabetes mellitus	3.63	0.053	3.18	0.075

infarction (15). Surprisingly, admission hemodynamic status was similar in the group of patients requiring emergency cardiac catheterization within 24 h to that in patients who did not require urgent evaluation. A history of diabetes mellitus was associated with a marginally greater risk of clinical instability. Previous studies (16–18) have noted a higher incidence of postinfarction angina, infarct extension, heart failure and a higher mortality rate in diabetic patients. Hematologic studies (19) have also suggested that diabetes may be associated with a hypercoagulable state characterized by increased platelet aggregability and impaired fibrinolytic activity. Other studies (20,21), however, have failed to show any relation between diabetes and infarct-related vessel reocclusion or reinfarction after thrombolysis.

The need for early intervention was relatively uncommon after combination thrombolytic therapy compared with that after monotherapy with rt-PA or urokinase alone. This difference may have been related to greater systemic fibrinolysis with combination therapy and greater generation of fibrinogen degradation products, both of which have been correlated with a reduced incidence of reocclusion (21). This finding is also consistent with the lower reocclusion rate of the infarct-related vessel after combined rt-PA and urokinase therapy observed in both the TAMI-2 pilot study (22) and in the cohort of patients assigned to the aggressive catheterization strategy of the TAMI-5 trial (1). The treatment regimen did not prove to be predictive, however, of the overall need for intervention within 5 days of admission. The possibility that combination thrombolytic therapy may have a salutary impact on early clinical outcome is currently being further examined in a very large, randomized, controlled clinical trial of rt-PA alone, streptokinase alone and combined streptokinase and rt-PA therapy (Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries trial).

In contrast to the TIMI-2B trial (23), in which coronary angiography and myocardial revascularization procedures were performed more frequently at sites with cardiac catheterization facilities, referral for urgent cardiac catheterization in our study was not dependent on the site of patient recruitment. However, the interpretation of this observation is limited by the variable referral patterns of the participating satellite sites. Whereas some community hospitals transferred patients as soon as possible to a main center, others admitted patients locally and transferred them to one of the main referral centers if their subsequent course became complicated or for diagnostic cardiac catheterization before hospital discharge.

Angiographic findings. Although all but two patients requiring urgent cardiac catheterization had recurrent ischemic chest pain or new ST segment elevation, only a minority (37%) had an occluded infarct-related artery (TIMI grade 0 or 1 flow) at the time of emergency cardiac catheterization. One-third of the patients had normal coronary flow in the infarct-related vessel. The majority (72%) had minimal or single-vessel disease. These findings highlight the previously described difficulties of accurate noninvasive determination of the patency status of the infarct-related vessel (24) and perhaps the frequent occurrence of intermittent reocclusion and spontaneous recanalization (25). The use of several potentially valuable noninvasive investigations, including cardiac isoenzyme determination (26) and continuous ST segment monitoring (27), is currently being studied and preliminary data are encouraging. If these tests can reliably determine infarct-related vessel patency, the need for emergency cardiac catheterization may be substantially reduced.

The need for intervention was not associated with infarction in the territory of any specific coronary artery. Infarct-related vessel reocclusion has been previously shown to occur more frequently after reperfusion of the right coronary artery (21,28), perhaps because of the larger caliber of the vessel, its slower flow and the relative absence of large side branches. However, in this study, the need for intervention was not more frequent in patients whose right coronary artery was identified as the infarct-related artery. One possible explanation for this observation is that any greater incidence of reocclusion in the right coronary artery was balanced by a greater incidence of hemodynamic compromise in patients with a left anterior descending artery-related infarct.

Impact of acute intervention on clinical outcome. The rationale for urgent angiographic evaluation of patients with recurrent myocardial ischemia or hemodynamic instability after thrombolytic therapy is to allow triage of patients to continued medical therapy or emergency myocardial revascularization if coronary flow is suboptimal. However, this approach has not been validated in a controlled randomized fashion. Rescue coronary angioplasty, for example, has been advocated (29) but has also been associated with a high incidence of reocclusion, particularly after rt-PA therapy (2,14), and with the potential to cause hemodynamic instability and life-threatening rhythm disturbances (30). Nonetheless, urgent coronary angiography does allow patients with severe triple-vessel or left main coronary artery disease to be triaged to early revascularization. The impact of this strategy on subsequent clinical outcome is difficult to evaluate. By definition, patients selected for urgent angiography in our study were at increased risk of in-hospital complications. It should not be surprising, therefore, that there was a trend toward a higher incidence of acute pulmonary edema in this group, worse global and regional left ventricular function and a higher in-hospital mortality rate. In the absence of a control group, the positive (or negative) impact of this strategy on clinical outcome remains speculative.

Limitations. Few data are available on the patients who developed recurrent myocardial ischemia or hemodynamic compromise but did not undergo urgent cardiac catheterization either because their condition was too unstable to permit transfer to the cardiac catheterization laboratory or because they died before transfer could be arranged. The actual number of patients, their management and subsequent

clinical outcome can, therefore, only be estimated, but the number of patients in this category is likely to be small.

Conclusions. In our study, urgent cardiac catheterization was frequently required after conservative postthrombolytic management, was poorly predicted by clinical variables and was associated with a relatively poor clinical outcome despite an aggressive approach to myocardial revascularization. These findings suggest that better adjunctive medical therapy is required to prevent infarct-related vessel reocclusion after successful reperfusion therapy. Furthermore, more reliable means of noninvasively identifying patients with a persistently occluded or reoccluded infarct-related artery are desirable and may obviate the need for invasive evaluation in a significant proportion of patients. Finally, randomized controlled trials may be necessary to determine the optimal method of treating patients with recurrent myocardial ischemia or hemodynamic instability after reperfusion therapy.

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